McNeil Consumer Healthcare, 7050 Camp Hill Road, Fort Washington, PA 19034-2299 (215) 273-7000

4915 99D-2635 C25

October 29, 1999

FDA Dockets Management Branch (HFA-305)
U.S. Food and Drug Administration
Room 1061
5630 Fishers Lane
Rockville, MD 20852

RE: Docket No. 99D-2635, Draft Guidance for Industry on ANDAs: Blend Uniformity Analysis; Notice of Availability and Request for Comments, Federal Register, August 27, 1999 (64 FR p. 46917)

Dear Sir or Madam:

Reference is made to the draft guidance published in the August 27, 1999 edition of the FEDERAL REGISTER concerning recommendations to applicants on establishing in-process acceptance criteria for blend uniformity analysis.

In response to this notice, enclosed for consideration are comments from McNeil Consumer Healthcare concerning this proposed draft guidance.

Thank you for this opportunity to respond. We trust that the enclosed information is in order. If you have any questions regarding this response, please contact me at (215) 273-8770.

Sincerely,

McNEIL CONSUMER HEALTHCARE

Ronald P. Torlini

Ronald P. Torlini
Director, cGMP Compliance

Enclosure

99D-2635

C25

McNeil Consumer Healthcare Comments on:
Guidance for Industry
ANDAs: Blend Uniformity Analysis
Published August 27, 1999
Federal Register Volume 64, No: 166, p. 46917

The pharmaceutical industry recognizes the importance of validating the final blend process during validation to ensure satisfactory active ingredient content in the final dosage form. However, once a process is validated, there is no longer a need for routine blend uniformity testing. In-process blend uniformity testing adds no value to the quality of the finished product.

During drug development, blend properties are evaluated along with sampling techniques. Blending operations have been well developed and validated. It is at this stage that additional sampling and testing is conducted to assure a robust final blend that ultimately leads to an acceptable finished product. Industry routinely provides these testing results to the agency during inspections. The acceptability of the finished product is substantiated by content uniformity release testing during routine manufacture.

It is important to note that blend uniformity testing should not be relied upon as a method of batch selection during routine production. No level of blend uniformity testing in the final blend can ensure compliance with USP acceptable criteria for content uniformity of the finished dosage form. During each transfer of the blend to the tablet die, the blend may pass through several areas including: valves, drums or bins, feed chutes, hoppers and feeders. Segregation mechanisms can manifest themselves at any time during this transfer resulting in failed content uniformity for a batch with acceptable blend uniformity OR acceptable finished product content uniformity for a batch with unacceptable blend uniformity results.

In addition, the draft guidance does not discuss common issues associated with sampling techniques of the final blend. This would be helpful for process validation work. For blend uniformity testing to be value added, these samples must be a true representation of the blend. Often their analysis is complicated by sampling error. Sampling errors are introduced by segregation via the design of the thief, sampling techniques and/or physical and chemical properties of the formulation. This guideline should provide alternatives to blend uniformity testing for those formulations, which do not lend themselves to normal sampling techniques. For example, during validation, additional finished product uniformity testing may be incorporated for products not meeting blend uniformity criteria.

It is our opinion that in-process blend analysis is necessary only as part of process development and process validation activities. This additional release criteria of performing in-process blend uniformity routinely at the final blend stage adds financial burden and provides no added value for a validated process.

523 Fairhill Road
Hatfield, PA 19440

McNeil
Consumer Healthcare

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